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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHONG, KIMBERLY	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
10/07/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,229	APOSTOLOPOULOS ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-98* is/are pending in the application.

4a) Of the above claim(s) *56,57 and 70-98* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-55,58-69* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 06/30/2010 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 12/30/2010 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 06/30/2010, claims 50-98 are pending. Claims 50-55 and 58-69 are currently under examination. Claims 56, 57 and 70-98 and non-elected species are withdrawn as being drawn to a non-elected invention.

New Claim Rejections

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 50, and 62-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Cotten et al. (US Patent No. 5,693,509).

The claims are drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide molecule, a carrier comprising at least one aldehyde group and a suitable linker and wherein the carrier comprises a plurality of aldehyde groups.

Cotten et al. teach an adenoviral delivery system for delivery of a DNA molecule to cells wherein the vector is conjugated to an oxidized transferrin molecule. Cotten et al. teach the transferrin comprises aldehyde groups which meets the limitation of a plurality (see columns 2 and 4).

Thus Cotten et al. anticipates the instant claims.

Claims 50, 52-55 and 62-65 are rejected under 35 U.S.C. 102(b) as being anticipated by Kircheis et al. (US 2002/0137670).

The claims are drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide molecule, a carrier comprising at least one aldehyde group and a suitable linker, wherein the carrier comprises a plurality of aldehyde groups, wherein the polynucleotide or oligonucleotide comprises an expression cassette comprising a promoter linked to a protein and wherein the protein is an antigen.

Kircheis et al. teach a complex comprising a DNA molecule that expresses a cytokine and a PEI molecule conjugated to an oxidized transferrin molecule for targeted delivery of the complex to tumor cells (see at least paragraphs 0028-0037, 0106 and 0131).

Thus Kircheis et al. anticipates the instant claims.

Claims 50, 52-55 and 62-65 are rejected under 35 U.S.C. 102(a) as being anticipated by Bellocq et al. (Bioconjugate Chem 2003, 14: 1122-1132).

The claims are drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide molecule, a carrier comprising at least one aldehyde group and a suitable linker, wherein the carrier comprises a plurality of aldehyde groups, wherein the polynucleotide or oligonucleotide comprises an expression cassette comprising a promoter linked to a protein and wherein the protein is an antigen.

Bellocq et al. teach targeted gene delivery using a complex comprising an oxidized transferrin molecule conjugated onto a nucleic acid molecule wherein the complex is delivered to tumor cells (see at least pages 1123, 1124).

Thus Bellocq et al. anticipates the instant claims.

New Claim Rejections - 35 USC § 103

Claims 50-55 and 58-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cotten et al. (US Patent No. 5,693,509), Wagner et al. PNAS 1990, Vol. 87: 3410-3414), Latham et al. Cancer Research 60, 334-341, January 2000 and Ming et al. (Pharmacology Reviews 2002, of record cited on IDS filed 09/22/2009).

The claims are drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide molecule, a carrier comprising at least one aldehyde group and a suitable linker wherein the polynucleotide is in the range of 5 bases to 10 kilobases, wherein the polynucleotide or oligonucleotide comprises an expression cassette comprising a promoter linked to a protein, wherein the protein is an antigen, , wherein

the carrier comprises a plurality of aldehyde groups, wherein the carrier is a ligand, wherein the carrier is an oxidized mannan and the linker is a polycation.

Cotten et al. teach an adenoviral delivery system for delivery of a DNA molecule to cells wherein the vector is conjugated to an oxidized transferrin molecule. Cotten et al. teach the transferrin comprises aldehyde groups which meets the limitation of a plurality (see columns 2 and 4) and further teach the transferrin ligand can allow targeting specific cells. Cotten et al. do not specifically teach the size of the polynucleotide or oligonucleotide, do not teach the polynucleotide comprises an expression vector for expression of an antigen, and do not teach the number of aldehyde groups in the carrier or that the DNA is conjugated to the carrier.

Wagner et al. demonstrates the use of a transferrin-polycation conjugate as carriers of DNA uptake in cells and teach the DNA complexed can be from short oligonucleotides to DNA of 21 kilobases (abstract) and this system can be used as an efficient delivery system to specifically target cells and deliver DNA into cells.

Latham et al. demonstrates it was well known in the art regarding the expression of an antigen from a vector, such as prostate specific antigen, using an adenoviral vector delivered to cells (see entire reference).

Ming et al. teach polycation linkers and methods of conjugation of molecules to DNA (see entire reference and pages 572-573).

It would have been obvious to one of ordinary skill in the art to use the delivery system taught by Cotton et al. for introduction of any size DNA as claimed into a specific cell and further obvious to deliver a DNA encoding an antigen as taught by Latham et al.

Cotten et al. do not teach the specific number of aldehyde groups of the transferrin molecule that is conjugated to the vector however it would have been routine to the skilled artisan to determine the specific amount of oxidized transferrin comprising aldehyde groups based on the efficiency of transfection of said complex into a targeted cell. It would have been obvious to link transferrin molecule to the DNA using a linker as polycation linkers for conjugation of DNA to ligands given Ming et al. teach methods of conjugation of carriers to DNA molecules.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 50-55 and 58-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sasaki et al. (Eur. J. Immunol. 1997, Vol. 27:3121-3129 of record), Apostolopoulos et al. (Eur. J. Immunol. 2000, of record cited on IDS filed 03/07/2008), Wagner et al. PNAS 1990, Vol. 87: 3410-3414) and Ming et al. (Pharmacology Reviews 2002, of record cited on IDS filed 09/22/2009)

The claims are drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide molecule, a carrier comprising at least one aldehyde group and a suitable linker wherein the polynucleotide is in the range of 5 bases to 10 kilobases, wherein the polynucleotide or oligonucleotide comprises an expression cassette comprising a promoter linked to a protein, wherein the protein is an antigen, wherein the carrier comprises a plurality of aldehyde groups, wherein the carrier is a ligand, wherein the carrier is an oxidized mannan and the linker is a polycation.

Sasaki et al. teach a compound comprising a DNA polynucleotide and a carrier comprising a mannan molecule, wherein the polynucleotide is in the claimed range (see paragraph 2.1 that references a previous report that describes making the DNA polynucleotide) and further teach the DNA comprises a promoter and encodes antigens that elicit an immune response in a cell. Sasaki et al. do not teach specifically teach the mannan is oxidized and comprises specific numbers of aldehyde groups.

Apostolopoulos et al. teach the use of oxidized mannan molecules that are conjugated to molecules wherein the mannan, which is recognized by a cell surface receptor, allows the complex to enter the cell more rapidly and direct subsequence immune responses more efficiently (see entire reference). Apostolopoulos et al. suggest that since the oxidized mannan conjugation produced such a strong response, this might be advantages when used with other antigens such as HIV and presents a major step forward in the production of vaccines (see page 10132). While Apostolopoulos et al do not teach the specific number of aldehyde groups of the transferrin molecule that is conjugated to the vector however it would have been routine to the skilled artisan to determine the specific amount of oxidized transferrin comprising aldehyde groups based on the efficiency of transfection of said complex into a targeted cell.

Ming et al. teach polycation linkers and methods of conjugation of molecules to DNA (see at least pages 572-573).

It would have been obvious to one of skill in the art at the time the invention was made to oxidize the mannan and use in a complex comprising the DNA vaccine given Apostolopoulos et al. teach the presence of the additional aldehyde groups allow for

more efficient entry into the cytoplasm of the cell and mediation of the immune response. One of skill in the art would have wanted to use the oxidized mannan with the compound taught by Sasaki et al. because Apostolopoulos et al. suggests this use could be advantageous when used with other HIV antigens, such as taught by Sasaki et al., for the production of vaccines. Moreover, it was well known in the art regarding the size of a polynucleotide or oligonucleotide that can be conjugated for use as a vaccine or for expression of a specific antigen as taught by Wagner et al. (discussed above) and therefore the size of the polynucleotide or oligonucleotide is by design choice and would be routine to one of skill in the art. It would have been obvious to link transferrin molecule to the DNA using a linker as polycation linkers for conjugation of DNA to ligands given Ming et al. teach methods of conjugation of carriers to DNA molecules.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 06/30/2010 have been fully considered but they are not persuasive. Applicant argues that Apostolopoulos does not disclose or suggest that oxidized mannan influences the efficiency of internalization and the conjugate of oxidized mannan is bound to a protein antigen rather than a polynucleotide or oligonucleotide. This argument is not convincing.

Applicants argue limitations that are not recited in the claims. The are drawn to a compound comprising a conjugate of a polynucleotide or oligonucleotide molecule, a

carrier comprising at least one aldehyde group and a suitable linker and wherein the carrier is an oxidized mannan and the linker is a polycation. The claims do not recite any functional language of the conjugate or that conjugation of a carrier provides any specific advantage or function to the polynucleotide or oligonucleotide and do not recite the mannan influences internalization of conjugate.

Apostolopoulos et al. teach the use of oxidized mannan molecules that are conjugated to molecules wherein the mannan, which is recognized by a cell surface receptor, allows the complex to enter the cell more rapidly and direct subsequence immune responses more efficiently. It therefore would have been obvious to one of skill in the art at the time the invention was made to oxidize the mannan and use in a complex comprising the DNA vaccine given Apostolopoulos et al. teach the presence of the additional aldehyde groups allow for more efficient entry into the cytoplasm of the cell and mediation of the immune response. The skilled artisan would have recognized this carrier as an efficient method to delivery molecules into cells more efficiently.

Response to Arguments

Claim Rejections - 35 USC § 102

The rejection of claims 50, 52 and 53 under 35 U.S.C. 102(b) as being anticipated by Sasaki et al. (Eur. J. Immunol. 1997, Vol. 27:3121-3129) is withdrawn.

Claim Rejections - 35 USC § 103

The rejection of claims 50, 52-55, 59-69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sasaki et al. (Eur. J. Immunol. 1997, Vol. 27:3121-3129) as relied upon above and in further view of Apostolopoulos et al. (Eur. J. Immunol. 2000, of record cited on IDS filed 03/07/2008), Liu et al. (Vaccine 20, 2002, pp 42-48) and Ming et al. (Pharmacology Reviews 2002, of record cited on IDS filed 09/22/2009) is withdrawn in view of the new grounds of rejection above.

Claims 50, 51 and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Azzam et al. (Macromol Symp. 2003 of record cited on International Search Report filed 05/12/2006) and Tuschl et al. (US 2004/0259247) is maintained for the reasons of record.

Applicant's arguments filed 06/30/2010 have been fully considered but they are not persuasive. Applicant argues that the oxidized dextran taught by Azzam et al. was converted to a dextran oligoamine conjugated by reduction and this was "presumably to ensure the dextran-oligoamine complex was fully reduced".

The argument is not convincing. Azzam et al. does not teach that the polyaldehyde dextran was reduced to remove all the aldehyde groups as presumed by applicant and this line of reasoning is not logical because Azzam et al. clearly teach a process for oxidizing dextran and measuring the amounts of aldehyde groups for use as a conjugate. To then reduce this conjugate to remove the aldehyde groups would mean the process of oxidizing would not have been needed. The claims at their broadest

require one aldehyde group and given was is taught by Azzam et al., the conjugate clearly meets this limitation and there is nothing in the reference to suggest the oxidized dextran conjugate does not contain any aldehyde groups.

The rejection is therefore maintained..

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful please contact Christopher Low at 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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